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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,324	06/29/2001	Bi-Yu Li	TM0011-UT	8386

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,324	LI ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action filed on September 3, 2003 has been entered and considered.

2. The Information Disclosure Statement filed on August 21, 2003 has been entered.

3. The instant application is filed on June 29, 2001, which claims priority to a provisional application No. 60/215,596, filed on June 30, 2000.

4. Claims 1-13, 15-21 are pending. Claims 14, 22-23 are cancelled.

Response to arguments

5. Applicants' response to the office action is fully considered and found persuasive.

6. With reference to the rejections made in the previous office action under provisional obviousness-type double patenting, Applicants' arguments with respect to claims 1-10, and 15-21 have been considered but are moot in view of the new ground(s) of rejection.

7. With reference to the rejections made in the previous office action under provisional obviousness-type double patenting, Applicants' arguments with respect to claims 1-13, and15-21 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1, 3-8, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato (USPN.5,707,807).

Kato teaches a method of claim 1 and 4, for amplifying a population of polynucleotides comprising

(a) reverse transcribing an RNA population to provide a double-stranded population (see column 4, lines 11-12);

(b) digesting said cDNA population with one or more restriction endonucleases (see column 4, lines 12-35) having a degenerate recognition ***or*** cleavage sequence, wherein the said restriction endonuclease is a three- to eight-base cutter (see column 7, lines 19-29, which include restriction endonucleases having degenerate bases) and wherein the degenerate recognition ***or*** cleavage sequence is represented by N^m where N is the extent of degeneracy (N is 2-4) and m is number of degenerate bases (m is 1-5) (restriction enzymes) produce different single stranded overhangs for each restriction endonuclease (see column 7, lines 30-35, lines 49-56, wherein cohesive ends are formed with a mixture of A, C, G, and T bases);

(c) ligating said fragments to a series of adaptors lacking restriction endonuclease sites (biotinylated adaptors having degenerate bases), wherein each adaptor is cohesive to all possible overhangs (see column 4, lines 14-21);

(d) amplifying said restriction fragments for 25 to 30 cycles which includes 25 cycles (see column 4, lines 54-61).

With regard to claim 3, Kato teaches said restriction endonuclease comprising four-base cutter (see column 7, lines 19-35);

With regard to claim 5, Kato teaches that the method uses a series of adaptors having a sequence complementary to overhangs (see column 7, lines 49-56);

With regard to claim 6, Kato teaches that said restriction fragments are amplified using PCR to produce PCR products (see column 6, lines 51-60);

With regard to claim 7, Kato teaches that said adaptors provide priming sites for PCR (see column 7, lines 66-67, column 8, lines 16);

With regard to claim 8, Kato teaches that the method comprises detection of PCR products using gel electrophoresis (see column 6, lines 57-60);

With regard to claim 15, Kato teaches that the method comprises total RNA (see column 4, lines 11-13).

Thus the disclosure of Kato meets the limitations in the instant claims.

B. Claim 1, 3-8, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by MacLeod et al. (USPN.6,221,600).

MacLeod et al. teach a method of claim 1 and 4, for amplifying a population of polynucleotides comprising

(a) reverse transcribing an RNA population to provide a double-stranded population (see column 55, lines 11-15, lines 29-31, lines 44-45, column 5, lines 18-25);

(b) digesting said cDNA population with one or more restriction endonucleases (see column 55, lines 11-21) having a degenerate recognition ***or*** cleavage sequence, wherein the said restriction endonuclease is a three- to eight-base cutter (see column 56, lines 37-54, which include restriction endonucleases having degenerate bases) and wherein the degenerate recognition ***or*** cleavage sequence is represented by N^m where N is the extent of degeneracy (N is 4-8) (see

column 6, lines and m is number of degenerate bases (m is 1-5) produce different single stranded overhangs for each restriction endonuclease (see column 19, lines 1-8, table.1, which provides restriction endonucleases consisting of degenerate bases 1-8);

(c) ligating said fragments to a series of adapters lacking restriction endonuclease sites (biotinylated adaptors having degenerate bases), wherein each adaptor is cohesive to all possible overhangs (see column 55, lines 22-23, column 33, lines 45-65);

(d) amplifying said restriction fragments (see column 55, line 24). MacLeod et al. also teach that the PCR was carried on with varying number of PCR cycles (from 24-27) and indicated exponential increase in the amount of amplifier produced for at least the 25^{th} through the 27^{th} cycle (see column 42, lines 50-67).

With regard to claim 2-3, MacLeod et al. teach that said restriction endonuclease comprising degenerate bases (m is 2-4) (see column 19, table.1) and four-base cutter (see column 56, lines 37-54, column 18, lines 54-65);

With regard to claim 5, MacLeod et al. teach that the method uses a series of adapters (linkers) having a sequence complementary to overhangs (see column 33, lines 45-65);

With regard to claim 6, MacLeod et al. teach that said restriction fragments are amplified using PCR to produce PCR products (see column 15, lines 65-67, column 16, lines 1-10);

With regard to claim 7, MacLeod et al. teach that said adapters provide priming sites for PCR (see column 34, lines 9-11);

With regard to claim 8, MacLeod et al. teach that the method comprises detection of PCR products (see column 6, lines 29-64);

With regard to claim 15, MacLeod et al. teach that the method comprises mRNA (see column 5, lines 19-25);

Thus the disclosure of MacLeod et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-13, 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLeod et al. (USPN.6,221,600) in view of McCasky Feazel et al. (USPN. 6,100,030).

MacLeod et al. teach a method of claim 9-13, 15-21, for amplifying a population of polynucleotides comprising

(a) reverse transcribing an RNA population to provide a double-stranded population (see column 55, lines 11-15, lines 29-31, lines 44-45, column 5, lines 18-25);

(b) digesting said cDNA population with one or more restriction endonucleases (see column 55, lines 11-21) having a degenerate recognition ***or*** cleavage sequence, wherein the said restriction endonuclease is a three- to eight-base cutter (see column 56, lines 37-54, which include restriction endonucleases having degenerate bases) and wherein the degenerate recognition ***or*** cleavage sequence is represented by N^m where N is the extent of degeneracy (N is 4-8) (see column 6, lines and m is number of degenerate bases (m is 1-5) produce different single stranded overhangs for each restriction endonuclease (see column 19, lines 1-8, table.1, which provides restriction endonucleases consisting of degenerate bases 1-8);

(c) ligating said fragments to a series of adapters lacking restriction endonuclease sites (biotinylated adaptors having degenerate bases), wherein each adaptor is cohesive to all possible overhangs (see column 55, lines 22-23, column 33, lines 45-65);

(d) amplifying said restriction fragments (see column 55, line 24). MacLeod et al. also teach that the PCR was carried on with varying number of PCR cycles (from 24-27) and indicated exponential increase in the amount of amplifier produced for at least the 25^{th} through the 27^{th} cycle (see column 42, lines 50-67). MacLeod et al. also teach that the method comprises mRNA (see column 5, lines 19-25). However, MacLeod et al. did not teach isolation of at least one PCR amplified product, cloning and expression of the said isolated PCR product, sequencing the PCR amplified product and comparison of the amplified product or expression pattern with a reference source.

McCasky Feazel et al. teach a method for high-throughput analysis of selective DNA fragment wherein McCasky Feazel et al. tech that the method comprises isolating amplified PCR product, cloning of the isolated amplification products (see column 9, lines 65-67, column 10,

lines 1-2, column 11, lines 23-47) and expression in appropriate host cells (see column 12, lines 34-55). McCasky Feazel et al. also teach sequencing of the amplified products and comparing the sequences or expression with a standard (see column 11, lines 49-67, column 12, lines 1-18, column 38, lines 10-28).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of amplification as taught by MacLeod et al. with the method of et al. McCasky Feazel et al. which is applicable to screen polymorphisms because McCasky Feazel et al. taught that the method would allow analysis of complex data and provide more DNA polymorphism data in less time and at lower cost and able to provide specific DNA markers (see column 3, lines 5-15). An ordinary practitioner would have been motivated to combine the method of MacLeod et al. with the high throughput assay system as taught by McCasky Feazel et al. in order to achieve the expected advantage of developing a high throughput method for screening a wide range of parameters as, polymorphism, and gene expression pattern because incorporation of the limitations taught by McCasky Feazel et al. would reduce cost and time and allows the development of a high-throughput analysis method.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary Benzion can be reached on 571-272-0782 . The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 22, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER